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HEMOGLOBINOPATHY IN BASRAH GOVERNORATE, CENTER STATISTICS AND NEW REGISTRY CHARACTERISTICS

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Abstract: A retrospective study that had been conducted depending on the patients records and center data bases, concentration on the evidence of registering new cases of the disease categories, a total of 8721 patients had been registered most of them was of sickle cell diseases categories (sickle cell anemia, sickle/β^+ and sickle/β^0) of 5954 (68.26%), thalassemia syndromes (27.71%). 52.11% are males and 47.78% are females with a male: female ratio of 1.09, most of them are of below 18 years old 4741 (54.34%) with an adult group of 3972 (45.54%), one third of them were illiterates the rest were educated of different levels, only 6% reached higher education. 1817 different hemoglobinopathy patients was registered in Basrah during the last five years, 27.6% of them were registered during 2019 alone, 39.8% of them were homozygous sickle cell diseases while heterozygous (sickle/β^+, sickle/β^0) represented 33.0% of all registered cases, thalassemia syndromes (thalassemia major, thalassemia intermedia and α thalassemia) were only 27.0%. **conclusions** Basra governorate contain a large cohort of hemoglobinopathies patients on the national level and new case detection and registry is still significantly high for the last five years although premarital screening program did conducted **recommendation** a more correlational and comparable studies are to be conducted to highlight different variables of the disease-specific characteristics and an evaluation is to be conducted on evidence based way for the outcome of the currently conducted premarital screening program.

Keywords: **:** Hemoglobinopathies, Basrah, Premarital Screening, Iraq

Introduction

1.1 Background

The most prevalent single gene illnesses in the world are known as hemoglobinopathies, or disorders of hemoglobin.(1)(2)

Two primary classifications exist for hemoglobinopathies: thalassemia syndromes, and sickle cell diseases which include 2 main variants ,homozygous sickle cell anemia and heterozygous sickle cell disease which may include many variants like S/β° ,S/β^+,S/D ,S/^{Punjab},ect .(3)

The World Health Organization estimates that hemoglobinopathies affect about 5% of the human population and that 300,000–400,000 infants are born each year with extremely dangerous hemoglobinopathies.[4][5]

The structural difference between valine and glutamic acid in the ß chain hemoglobin molecule is The cause of SCD symptoms.[3] Due to this modification, red blood cells acquire characteristic "sickle" shapes, and when they are exposed to reduced oxygen concentrations, their surfaces bind one another and result in polymerization. The consequences of this “small” difference in the RBC structure that causes polymerization include immune system changes, ischemia, or decreased blood supply to essential organs, as well as chronic obstruction of blood arteries. Hemolytic anemia also results from the aberrant sickle cells being eliminated from circulation too soon. Transfusion is an essential component of the treatment for some SCD issues. It's also a method to prevent some of these adverse consequences from happening.[6]

Defects in any amount of hemoglobin chains' synthesis can cause thalassemia. While beta thalassemia is caused by reduced or absent beta chain of globin synthesis, alpha thalassemia is caused by decreased or absent alpha globin chain synthesis. An imbalance in the globin chains interrupts erythropoiesis and results in hemolysis. People with alpha or beta thalassemia trait and silent carriers of the disease are asymptomatic and don’t need medical attention. The main cause of hemolytic anemia, stunted growth, and aberrant skeletal development in infants is beta thalassemia, which need frequent lifetime blood transfusions. Compared to beta thalassemia major, beta thalassemia intermedia is less severe and may need periodic blood transfusions.[7]

1.2 Global and regional prevalence

According to estimates from the World Health Organization, carriers of different inherited hemoglobin problems make up around 7% of the world's population, making them the most prevalent types of recessive genetic illnesses.[8]

With 4.4 per 10,000 live births, thalassemia is one of the most prevalent hereditary hemoglobinopathy in the world. The East Mediterranean area has a higher frequency of β-thalassemia (9.0 per 1000).[9]

Ultimately, though, there are regional variations in the occurrence of β-thalassemia, with larger rates seen in some areas. Because of genetic factors and history migratory patterns, there is a high frequency of β-thalassemia in the region of the Mediterranean (including Greece, Italy, and and Cyprus), the Middle East (including Iraq, and Saudi Arabia), and portions of Asia (which incorporates India, Pakistan, and Bangladesh).[10]

Conversely, SCD distribution is extensive in African nations, including the southern Sahara, the Middle East, the nation of India, and those of African descent residing in Europe, North America, Central America, and South America.[11] While the global number of sickle cell disease births increased by 13.7% to 515 000 (425000–614,00000) between 2000 and 2021, mostly as a result of growth in population in the Caribbean and westerners and central sub-Saharan Africa, national incidence rates of the disease remained comparatively stable during that time. Sickle cell illness affected 5.46 million (4.62–6.45) persons globally in 2000; by 2021, that number had risen to 7.74 million (6.51–9.2), a 41.4% (38.3–44.9) increase.[12]

Across the world, the Middle East is considered one of the regions with the highest rates of hemoglobinopathies, along other. For example, Saudi Arabia is one of those countries. In a study conducted by using collected data from February 2011 to December 2015, through 125 centers across all the Saudi Kingdom, it found that the overall prevalence rate of SCT was 45.8 per 1000, and 3.8 for SCD. While for β thalassemia the prevalence rate was 12.9 per 1000 for the trait and 0.7 per 1000

for β thalassemia major. Of a total of 12,30,582 individuals that go throughout the study with positive test.(13)

Hemoglobinopathies are also relatively common in Oman; a research using data from 19 hospitals found that the frequency of thalassemia was 0.4 per 1000 people and SCD was 2.7 per 1000 people. of a 1,450,000 person population sample.(14)

Unlike in Saudi Arabia and Oman, a 11-year study in Kuwait shows that thalassemia is more prevalence than SCD, with prevalence of 21.1 and 18.1 per 1000 respectively, although most of the cases of thalassemia trait rather than β Thalassemia. The total population sample was 275,819.(15) Conclusively, despite several attempts at prevention and mitigating the impact of these illnesses, there is a significant incidence in the Middle Eastern countries.

1.3 National prevalence

On the national level, despite no large study that analyzes the data across all the centers on the national level except for a few ones, most of the other studies data are within the scope of its center or the majority of the population sample are limited to of its governorate's. This research will provide the most recent, large scale data when available.

In general, one of the last recent studies indicates that the prevalence of thalassemia, through the data within 16 thalassemia centers in Iraq, was 37.1 per 100,000 in 2015. Between 2010 and December 2015, 11,165 cases of thalassemia were diagnosed, accounting for 66.3% of all hereditary anemia cases that were registered at these facilities. Which consider a significant rate with the need of attention and awareness to this hereditary disease and its burdens on our community.(16)

On the governorates distribution, a lot of studies had been held to elicit the prevalence within their population although separately. For instance, a study in the thalassemia center of Al-Najaf governorate, and by using the collected data of 1,122 patients from October 2019 to March 2020, it concluded that beta thalassemia is the number one diagnosed condition among the hereditary hematologic disorders and accounting for 33.15% of the patients registered in the center in duration of the study. In comparison, SCD account only for 9%.(17)

Another study in Erbil, northern Iraq, also found that beta thalassemia is the dominant condition among the hemoglobinopathies within their population, with a percentage as high as 78.71%. While the SCD account only for 6.23%. Overall, the peak age was between 6-15 years account for 44.45%, following by 23.20% for the age group from 1-5 years. The 6-year study showed a steadily increase with all the hemoglobinopathies cases each year.(18)

After the initial reports of sickle-cell disease and thalassemia major from Iraq in the early 1960s, these hereditary disorders gained national recognition as serious health issues, leading to the establishment of centers for their management across the nation.(19)(20)

These studies conclude that the prevalence of both thalassemia and SCD vary differently depending on the center population. But as a general, the prevalence considers high otherwise.

1.4 Role of premarital screening

Premarital screening is considered the primary preventative measure for couples planning a child, a crucial step in maintaining society and allowing people to enjoy life, and a means of reducing the occurrence of inherited blood illnesses such hemoglobinopathy (21, 22,23).

In order to lower the morbidity and death rate associated with hemoglobinopathies, the World Health Organization (WHO) recommended member states to establish national programs for care and prevention of these illnesses in 2006.(24)(25)

The goal of WHO is carrier identifying and genetic counseling with provision of effective measures to reduce these births. Consanguineous marriages are very common in Iraq (47% - 60%).[26] Based on the effective model used by Cyprus or the Islamic Republic of Iran, the proposed preventative program would involve premarital screening, counseling, and prenatal diagnosis.[27][28] Although a premarital hemoglobinopathy screening program may be warranted in our area, it should be highlighted that there are a number of obstacles to the program's complete effectiveness. Premarital screening is only done a few days before the wedding and not during the engagement phase, which is one of these constraints. Another is the prevalence of arranged and consanguineous marriages. Even after receiving the proper genetic counseling, these two considerations makes the notion of separation difficult and socially undesirable for couples who are discovered to be at risk. Conflicting findings have been published in the past about the real effects of genetic counseling on at-risk couples throughout the world. As a result, although some have claimed it has no impact, others have argued that in roughly half of these cases, it could result in separation.[28]

1.5 Basra previous studies

Our community has a high prevalence of sickle cell and thalassemia disorders, and the Basra Centre for Inherited Blood Disorders is one of the biggest centers for this condition in Iraq.
Numerous diverse blood illnesses that are all classified as hereditary can be found in the Basra Centre for Hereditary Blood illnesses, whilst that the carrier state for both thalassemia (4.6%) and the frequencies of sickle cell trait prevalence vary greatly in different regions of Iraq (0.06–0.07%) in the North whilst it is in its extreme maximization (6.5%) in Basrah.[29] . The time trend of the newly registered patients in Basrah did show an accelerated increment in 2019, with the registration of about 606 new patients differing slightly from that of thalassemia. Iraqi trend for the last five years was published in an Iraqi study in which a steady increase did exist. This acceleration was explained by the demand for registration in order to be included in social care after the adoption of the Social Care Law for patients with haemoglobin disorders in Iraq. Again the most predominant newly registered were male gender, sickle cell diseases, patients from peripheries and below five years age groups.[30]

Hemoglobinopathies And Socioeconomic Aspects

Way of life and standard of living Individuals with thalassemia who acquire the highest quality of care can now lead almost normal lives while experiencing complete mental and physical growth from childhood to adulthood, despite the fact that TDT is a burdensome condition that requires close monitoring, lifelong treatment, and follow-up. Complications caused by many different systems can often complicate TDT cases.[31]

Unfortunately, low- or middle-income nations account for over 80% of all children born with these illnesses each year, and many of these economies lack the necessary infrastructure to adequately control and manage these conditions.[32]

The World Health Organization (WHO) has proposed a 50% reduction in medication-related harm in order to support effective and sustainable healthcare. Regulatory bodies have placed a greater emphasis on pharmacovigilance, and drug availability, feasibility, and minimal adverse reaction all play a significant role in adherence by patients and wellbeing. Research Objectives:

1. To elaborate the statistical situation of hemoglobinopathy in Basrah
2. To elicit evidence of new case detection in Basrah regarding hemoglobinopathy.
3. To study certain characteristics of the newly diagnosed cases.

Methods

A retrospective study that had been conducted depending on the patients records and center data bases had been obtained from the BCHBD after a written approval , data had been processed as numbers and percentages for obtaining the study objectives in highlighting the current situation for hemoglobinopathy in Basrah governorate beside the new patient registry characteristics.

Population: all hemoglobinopathy cases registered from January 2019 till the end of December 2023 in Basra center for hereditary blood diseases, hereditary bleeding disorders, query hereditary natures and odd diagnosis had been excluded.

Data: patients data from electronic data base of the center is to be selectively taken, tabled, and analyzed and graphed all in descriptive, non comparative design that was sufficient to yield the study objectives.

Software: numbers and percentages and graphs all ere set and processed by Microsoft office professional plus excel 2019 ®

Results and Discussion

Table (1) overall center cases registry statistics with demographic distributions

Variables	No.	Percentage to total
Diagnosis		
Thalassemia major	1365	15.65%
Thalassemia intermedia	499	5.72%
α thalassemia	553	6.34%
Sickle cell anemia	2808	32.19%
Sickle/β^+	1451	16.63%
Sickle/β^0	1695	19.44%
Others	350	4.01%
Total	8721	100%
Sex distribution		
Male	4545	52.11%
Females	4167	47.78%
Age (years) distributions		
0-5	845	9.68%
6-12	2548	29.21%
13-18	1348	15.45%
>18	3972	45.54%
Residency		
Centre	3707	42.50%
Periphery	5014	57.50%
Education level		
Illiterate	2871	33%
Primary	2457	28%
Secondary	2862	33%

A very large cohort of hereditary blood diseases are recorded in BCHBD

A total of 8721 patient had been registered most of them is sickle cell diseases categories (sickle cell anemia, sickle/β^+ and sickle/β^0) of 5954 (68.26%) followed by thalassemia categories (thalassemia major, thalassemia intermedia and α thalassemia) of 2417 (27.71%). 52.11% are males and 47.78% are females with a male: female ratio of (1.09), most of them are of below 18 years old 4741(54.34%) with an adult group of 3972 (45.54%), 57.5 % are from the peripheries and 63.41% were a product of a consanguineous marriage, one third of them were illiterates the rest were educated of different levels, only 6% reached higher educational institutes.

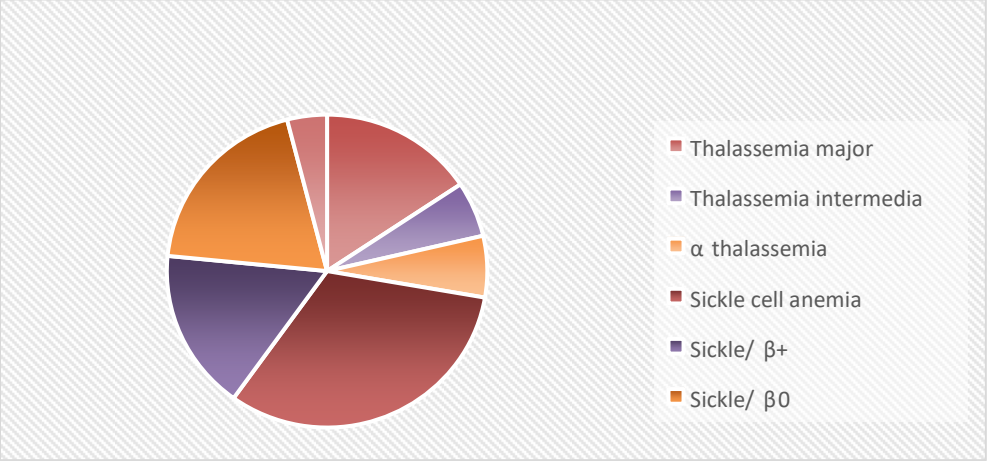
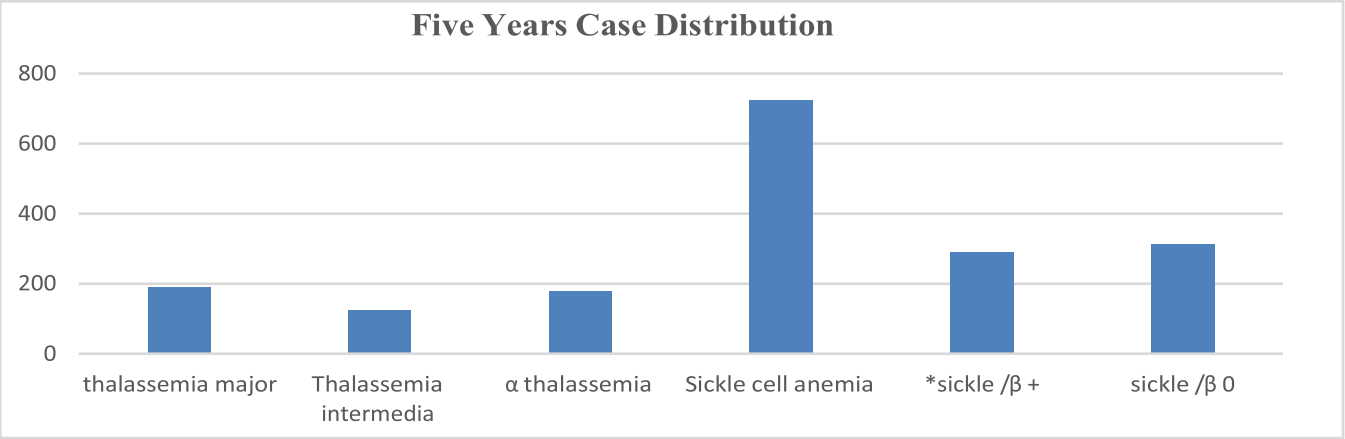


Table (2) five years new case distribution according to the type of hemoglobinopathies*

Diagnosis	2019	2020	2021	2022	2023	Total
Thalassemia major	42	36	41	29	41	189(10.40%)
Thalassemia intermedia	44	16	16	29	19	124(6.82%)
α thalassemia	39	36	38	40	26	179(9.85%)
Sickle cell anemia	194	164	108	128	130	724(39.85%)
***Sickle/β^+**	79	64	34	35	77	289(15.91%)
Sickle/β^0	104	70	61	59	18	312(17.17%)
Total	502(27.63%)	386(21.24%)	298(16.40%)	320(17.61%)	311(17.12%)	1817(100%)

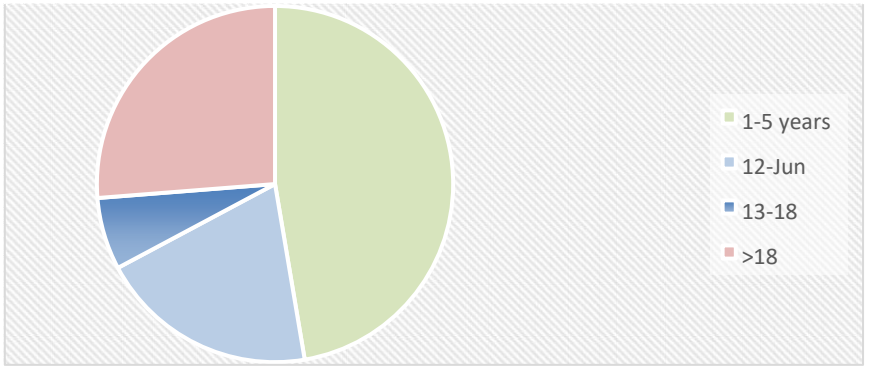
* Only major hemoglobinopathies was calculated ,only new registration included



Graph (1) new cases registered during last five years according to the type of hemoglobinopathy 1817 different hemoglobinopathy patient was registered in Basrah during the last 5 years, 27.6% of them were registered during 2019 alone, 39.8% of them were homozygous sickle cell diseases while heterogeneous (*sickle/β^+, sickle/β^0) represented 33.0% of all registered cases, thalassemia syndromes (thalassemia major, thalassemia intermedia and α thalassemia) were only 27.0%.

Table (3) case distribution of the new registered cases according to the age categories

Year	1-5	%	6-12	%	13-18	%	>18	%	totals	% years
2019	219	43.63%	93	18.53%	40	7.97%	150	29.88%	502	27.63%
2020	124	24.70%	53	10.56%	30	5.98%	179	35.66%	386	21.27%
2021	150	29.88%	41	8.17%	5	1.00%	102	20.32%	298	16.42%
2022	180	35.86%	74	14.74%	20	3.98%	46	9.16%	321	17.64%
2023	187	37.25%	100	19.92%	24	4.78%	0	0.00%	311	17.12%
Total	860	47.33%	361	19.87%	119	6.55%	477	26.25%	1817	1 00

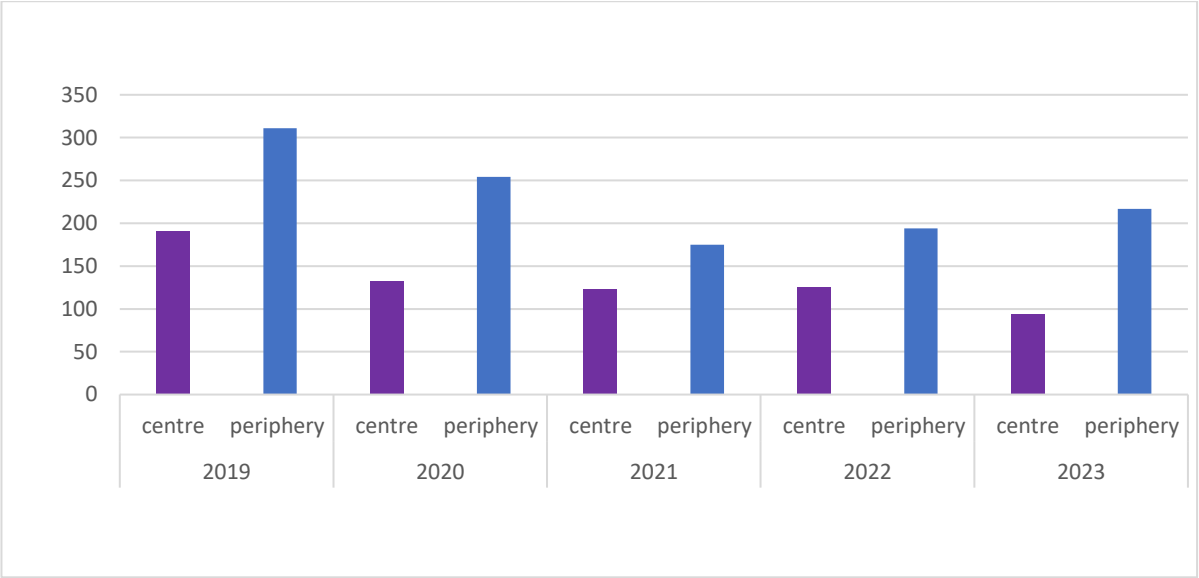


Graph (2) case distribution of the new registered cases according to the age categories

Most of the registered cases (47.3%) were belong to the <5 years age, adults represent (26.2%) only. **Table**

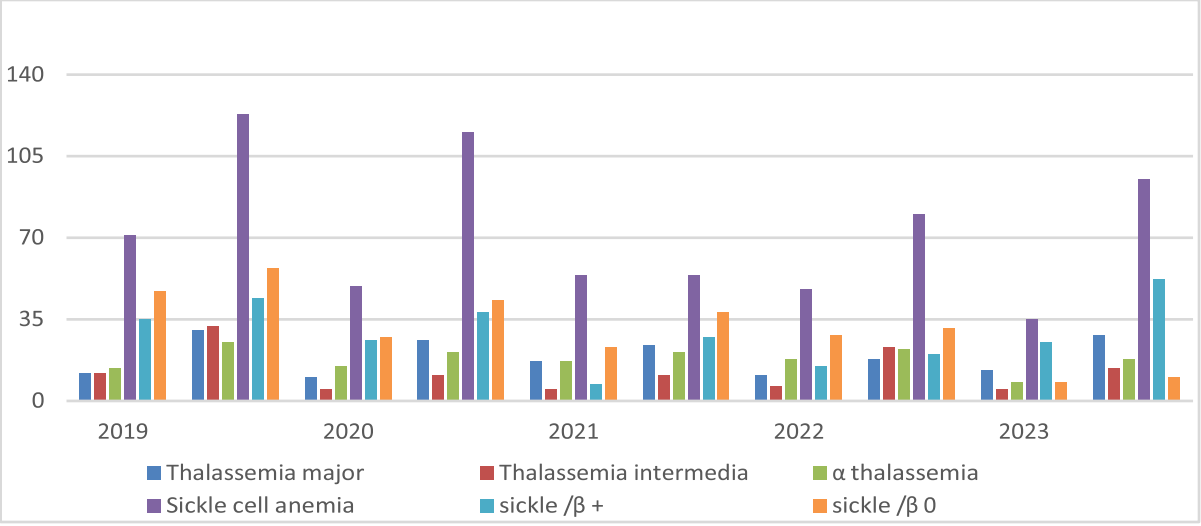
(4) five years case distribution according to the residency and type of hemoglobinopathies

Year	**2019**		**2020**		**2021**		**2022**		**2023**		**Total**	
Residency	center	periphery	center	periphery	center	periphery	center	periphery	center	periphery	center	periphery
Thalassemia major	12	30	10	26	17	24	11	18	13	28	63	126
Thalassemia intermedia	12	32	5	11	5	11	6	23	5	14	33	91
α thalassemia	14	25	15	21	17	21	18	22	8	18	72	179
Sickle cell anemia	71	123	49	115	54	54	48	80	35	95	436	467
Sickle/β⁺	35	44	26	38	7	27	15	20	25	52	108	181
Sickle/β⁰	47	57	27	43	23	38	28	31	8	10	133	312
Total for residency	191	311	132	254	123	175	126	194	94	217	666	1151
	10.51%	17.12%	7.26%	13.98%	6.77%	9.63%	6.93%	10.68%	5.17%	11.94%	36.65%	63.35%
Annual total	502		386		298		320		311		1817	



Graph (3) five years case distribution according to the residency

Over the five years distribution most of the newly registered cases were from the peripheries.



five years case distribution according to the residency

Graph (4) five years case distribution according to the residency and type of hemoglobinopathies Most of the thalassemia categories were from peripheries 70.2% of the total thalassemia registry, whilst 58.6% of the sickle cell diseases were from the peripheries.

Discussion

The Basrah Centre for Hereditary Blood disorders is one of the biggest hematology centers in the country, with a wide range of disorders registered there, A total of 8721 patient had been registered most of them is sickle cell diseases categories (sickle cell anemia sickle /β^+ and sickle/β^0) of 5954 (68.26%) followed by thalassemia syndromes (27.71%). 52.11% are males and 47.78% are females with a male:female ratio of 1.09, most of them are of below 18 years old 4741 (54.34%) with an adult group of 3972 (45.54%), one third of them were illiterates the rest were educated of different levels, only 6% reached higher educational institutes.

Similar gender-related traits were discovered in a large Saudi investigation, involving a sample of 7054 patients, of which 3822 (54.2%) were male and 3232 (45.8%) were female. The planned study's findings demonstrated Saudi Arabia's high prevalence of β-thalassemia (12.8%) and sickle cell anemia (30.7%). In this study, the hemoglobinopathy that occurred most frequently was sickle cell disease. [(33)], whilst the figure is greatly different from other parts in Iraq in which thalassemia is almost the predominant like Najaf, that showed a greatly different in regards to the type distribution, as sickle cell disease was greatly less frequent, whereas in Najaf City, there are 69.60 hemoglobinopathies for every 100,000 people. The three most common disorders were sickleβ thalassemia disorder (13.746%), non-transfusion-dependent thalassemia (34.656%), then transfusion-dependent thalassemia (36.012%). A similar sex distribution was found in the same series[(17)] , In comparison to other studies in India, Tribal, In our study, there were 16,133 (24.53%) male cases and 41,624 (63.28%) female cases, respectively. [(34)(35)], While some research indicated a male predominance, documented literature demonstrates an equal proportion for males and females among hemoglobinopathy carriers[(34)(35)]. In Al Najaf, however, there are noticeably more male patients than female patients (54.37% male, 45.63%).[(17)]

According to national data provided by Kadhem et al. in 2017, more than half of the cases that were registered were under the age of 15, meaning that 57.5% of the cases originated from the periphery and 63.41% were the result of consanguineous marriages. Simulating results were shown in other series in the world, like in Brazil and India [(36)(37)], According to an Iraqi study, 78.8% of the patients reported having related parents, and roughly 66.0% of the individuals were under the age of fifteen (consanguineous marriage). [(17)].

The time trend of the newly registered patients in Basrah did show an accelerated increment in 2019, with the registration of about 606 new patients differing slightly from that of thalassemia. Iraqi trend for the last five years was published in an Iraqi study in which a steady increase did exist. This acceleration was explained by the demand for registration in order to be included in social care after the adoption of the Social Care Law for patients with haemoglobin disorders in Iraq[(38)(39)]. Again the most predominant newly registered were male gender, sickle cell diseases, patients from peripheries and below five years age groups, a similar program conducted in nearby countries did show more successful outcomes like in Kuwait where the initiative was successful in stopping 50.4% of risky couples from getting married by giving unsafe marriage certificates, according to the program's data. To better achieve the program's primary goal of reducing high-risk marriages, further work is still required[(15)]. This partial futility of the premarital screening program in our locality my be partially explained by the social rules and community stubbornness. This assertion is based on how the populace behaves culturally when adjusting to new laws and customs that are followed or handed

down from one generation of people to the next. The topic of marriage is important to cultural and religious norms, therefore unless there was a law requiring science to be used in the process, society would not have complied with the new pre-testing regulations.[40], On the other hand, β-thalassemia screening has led to a greater than 95% reduction in the birth prevalence in Cyprus[41], and comparable achievements for Sardinia were discovered[42] and Turkey[43]. Some country, like Saudi Arabia, Bahrain, and Iran, have made premarital screening programs publicly available, with some of these initiatives focusing on prevention[44]. Nevertheless, because some couples marry even after receiving a diagnosis of being carriers and because there aren't enough prenatal diagnostic programs, these initiatives haven't always resulted in fewer affected births [44],[45]

Conclusion

1. Basra governorate contain a large cohort of hemoglobinopathies patient on the national level.
2. New case detection and registry is still significantly high for the last five years although premarital screening program did conducted.
3. Disease categorization is greatly differs from other locality in Iraq in a form of sickle cell disease predominancy in Basrah.

Recommendations:

1. larger multicenter studies to be conducted to elaborate the national situation of hemoglobinopathies.
2. More correlational and comparable studies are to be conducted to highlight different variables of the disease-specific characteristics.
3. An evaluation is to be conducted on evidence based way for the outcome of the currently conducted premarital screening program.

Limitations:

The limitation of the current study is the descriptive study design, single center and the retrospective pattern of data gathering. A larger multi center and comparative study design is needed to highlight the disease increment and epidemiological variables on the base of collaborative multicenter base.

Conflict of interest

Each author states that there is no conflicts of interest and that there are no personal situations that could improperly affect how research findings are presented or interpreted.

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